REMARKS

Applicants thank the Examiner for the courtesies she and her supervisor extended to applicants' representatives during the interview held on April 24, 2007. During applicants representatives explained that the claimed invention is not inconsistent with written by Risbridger. During the interview, the Examiner and her supervisor agreed that the arguments presented by applicants' representatives seemed to overcome the pending rejection. The Examiner, however, requested that the arguments be made in a written response. In accordance with the Examiner's request, following is the requested written response.

Claims 58, 60, 62, 63, 69, 72-91, 93 and 95-99 stand rejected under 35 USC 112 first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner states that the article written by the co-inventor of this application contradicts "the claimed invention and thus, one skilled in the art would not know how to practice the claimed method and would be forced into under [sic] experimentation for use a [sic] a method of screening a mammal for prostate cancer by detecting the levels of inhibin."

As explained below and as discussed during the interview, the article written by Risbridger, does not contradict the claimed invention.

The Examiner is alleging that the invention is not enabled on the basis that the Risbridger article indicates the opposite conclusion to that claimed in the present application. Specifically, the Examiner alleges that since this prior art document discloses patients in which there was an increase in inhibin levels in prostate cancer, that this does not support and is not consistent with the claimed invention that a down regulation in inhibin levels is indicative of prostate cancer. Accordingly, the Examiner is alleging that one would not be able to successfully detect or screen prostate cancer by looking for a down regulation or absence of inhibin protein.

As explained during the interview, "cancer" is a word which does not describe a disease with a single phenotype. Rather, it describes a disease which exhibits a range of phenotypes reflecting the fact that cancer is a progressive disease. Accordingly, it is now clearly understood that prostate

cancer commences as a low grade cancer which eventually progresses to a moderate grade and thereafter to a high grade. High grade cancer can progress into metastatic cancer. It is important to note that even within each of these three broad "grade" categories there is a progression which occurs and which is reflected by the fact that within a single grade there is a range of progressively increasing Gleason scores which apply. Gleason scores are articulated on a scale of 1-10 and are determined based on the sum of two Gleason grade results (Gleason grades are numbered 1-5).

Not all high grade cancers are metastatic. Even among moderate grade cancers, some will progress to become aggressive cancers and some will not. Accordingly, there is the potential for significant variation from one cancer to the next in terms of its phenotype and progression. Further to this, it is also now understood that although inhibin levels do decrease below normal levels at the onset of prostate cancer and during its earlier stages, when some of these cancers progress to become aggressive cancers which may or may not have metastasized, there can occur a change to inhibin expression and functionality with the below normal level of inhibin expression rapidly increasing to well above normal levels of inhibin once these cancers progress along the metastatic path.

The Risbridger article cited by the Examiner represents the initial publication which noticed and commented on this phenomenon. However, this change to inhibin levels in certain highly aggressive cancers (but not necessarily all high grade cancers) was not fully elucidated at this point - this being the reason that the authors noted that further analysis/study was required. As discussed in the interview, it is important to note that the low, moderate or high grade classification of the cancer is not itself conclusive of whether the cancer is aggressive or not or whether it will become metastatic. Accordingly, discussion in relation to the three broad "grades" of cancer must take into account that there can be significant variation to the relative stage or aggressiveness of cancer falling within that "grade" of low, moderate or high.

In terms of the Examiner's rejection, as explained during the interview, the Examiner is initially approaching the analysis of the claimed invention from the wrong perspective. Specifically, it would appear that the Examiner is assuming that we are claiming that all prostate

cancers are characterized by a decrease in inhibin levels and are therefore diagnosable by virtue of screening for a decrease in inhibin levels. However, the claims are not directed to diagnosing prostate cancer, per se. Rather, they are directed to a method of screening a mammal wherein if one observes a decrease in inhibin protein level, then this is regarded as indicative of the mammal having developed prostate cancer. This is a significantly different position to that which the Examiner implies has been claimed since the claims as currently pending are not suggesting that all prostate cancers are diagnosable by virtue of screening for a down regulation of inhibin levels. Rather, they are indicating that where one observes a decrease in inhibin levels, this is indicative of that patient having developed prostate cancer. Accordingly, it is conceivable that there may exist patients in whom the inhibin level is not decreased, such as a patient who is transitioning to metastatic prostate cancer, who would not be detected by the method of the invention. However, the central issue is that for patients who exhibit a decrease in inhibin level, this is indicative that those patients have developed prostate cancer.

Accordingly, the scientific correlation between a decrease in inhibin levels and the onset of prostate cancer is true and correct across patients in whom a decrease in inhibin levels is observed. The Risbridger article indicates that there also exist patients in whom inhibin levels eventually become increased above normal, these being patients who are transitioning to metastatic prostate cancer, merely clarifies that the claimed invention usefully and accurately detects a subgroup of patients who have developed prostate cancer. The invention as claimed is consistent with this and does not claim the diagnosis of prostate cancers.

Accordingly, it was submitted to the Examiner that the claims are not drawing a correlation wherein all prostate cancers are associated with a down regulation in inhibin levels and therefore prostate cancer is diagnosable by screening for a down regulation in inhibin levels. Rather, the claims are drawing a correlation between the occurrence of a down regulation in inhibin levels and the fact that where this does occur, this is indicative of prostate cancer. The focus is therefore on the existence of a down regulation in inhibin, and what that means in terms of the onset of prostate cancer, rather than on the diagnosis of all prostate cancers.

It is also important to note that not all patients who develop prostate cancer may necessarily go on to develop metastatic cancer. Some patients may remain at a lower grade stage or others may progress through to a moderate or even high grade stage but not necessarily a metastatic stage. As a cancer does progress through the moderate grade to the high grade and ultimately to a metastatic stage, there occurs not just a shift in the phenotype of the cancer but, further, a switch in terms of the functionality of the inhibin molecule. Specifically, as the cancer progresses into a highly aggressive state, inhibin levels are observed to become increased above normal levels. This is not inconsistent with the present application which merely discloses and claims the observation that levels of inhibin below normal are indicative of a mammal having developed prostate cancer. This remains indisputable and is reproducible. The fact that highly aggressive cancer may not be detected by this method, since inhibin levels are in fact increased above normal levels at this time, merely indicates that one particular subgroup of prostate cancers will not be diagnosed by this method.

This being the case, the claimed invention is entirely consistent with the Risbridger article, which merely presents the early data that ultimately led to the elucidation of the finding that inhibin levels do change at the time that a prostate cancer becomes highly aggressive, this being referred to as a "switch". This switch hypothesis has in fact been significantly further analyzed and refined and, as discussed in the interview, is itself the subject of a separate patent application directed to screening for the development of metastatic prostate cancer. These findings do not change the fact, however, that a decrease in inhibin levels below normal is indicative of a patient having developed prostate cancer.

The Examiner has also noted at page 3 of the Office Action that Example 14 of the specification teaches that patients with a high Gleeson score did not exhibit inhibin expression. The Examiner argues that this is inconsistent with the Risbridger article, which indicates that there is a switch in the function and expression of inhibin molecules in advanced cancer and that the switch to a metastatic state is associated with an increase in inhibin levels. As discussed in the interview, there is in fact no inconsistency in this in that a high Gleeson score cancer which is not metastatic may not yet have undergone the switch in inhibin expression levels, which the article indicates is

indicative of the shift to a highly aggressive metastatic state. The fact that the prior art document indicates that the role of inhibin as a tumor suppressor requires re-evaluation is also not inconsistent with the present invention but merely indicates that the inventors have uncovered a degree of complexity in terms of the functioning of inhibin and that in fact the progression of prostate cancer can be delineated in more detail than was previously understood and therefore warrants further study. It docs not, however, render incorrect or inconsistent the original findings that prostate cancer onset is associated with a decrease in inhibin levels and that wherever one does detect a decrease in inhibin levels, this is indicative of that patient having developed prostate cancer.

Finally, during the interview the Examiner and her supervisor also indicated that it was highly relevant and very important to the patentability of the claims that the claims were couched in terms of a decrease in inhibin levels being "indicative" of cancer, rather than the claims being couched in terns of the diagnosis of all prostate cancers being associated with a decrease in inhibin levels.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and

authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing Attorney Docket No. **229752000800**.

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Respectfully submitted,

By_____

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